
Pleiotrophin Regulates the Retention and Self-Renewal of Hematopoietic Stem Cells in the Bone Marrow Vascular Niche.

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Public Summary:

The mechanisms through which the bone marrow (BM) microenvironment regulates hematopoietic stem cell (HSC) fate remain incompletely understood. We examined the role of the heparin-binding growth factor pleiotrophin (PTN) in regulating HSC function in the niche. PTN(-/-) mice displayed significantly decreased BM HSC content and impaired hematopoietic regeneration following myelosuppression. Conversely, mice lacking protein tyrosine phosphatase receptor zeta, which is inactivated by PTN, displayed significantly increased BM HSC content. Transplant studies revealed that PTN action was not HSC autonomous, but rather was mediated by the BM microenvironment. Interestingly, PTN was differentially expressed and secreted by BM sinusoidal endothelial cells within the vascular niche. Furthermore, systemic administration of anti-PTN antibody in mice substantially impaired both the homing of hematopoietic progenitor cells to the niche and the retention of BM HSCs in the niche. PTN is a secreted component of the BM vascular niche that regulates HSC self-renewal and retention in vivo.

Scientific Abstract:

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